```
     FILE 'REGISTRY' ENTERED AT 12:30:17 ON 12 JUN 2009
                EXP DIOXOLANE THYMINE/CN
L1              STRUCTURE UPLOADED
L2            8 S L1

     FILE 'STNGUIDE' ENTERED AT 12:31:38 ON 12 JUN 2009

     FILE 'REGISTRY' ENTERED AT 12:32:44 ON 12 JUN 2009
L3              STRUCTURE UPLOADED
L4            1 S L3
L5           70 S L3 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 12:33:09 ON 12 JUN 2009
L6           16 S L5/THU
L7       137840 S HIV OR (HUMAN IMMUNODEFICIENCY VIRUS) OR AIDS OR K65R OR M184
L8           14 S L6 AND L7
```

```
=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22

FILE 'REGISTRY' ENTERED AT 12:30:17 ON 12 JUN 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   10 JUN 2009  HIGHEST RN 1155458-91-5
DICTIONARY FILE UPDATES:  10 JUN 2009  HIGHEST RN 1155458-91-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> exp dioxolane thymine/cn
E1            1     DIOXOLANE POLYMERS/CN
E2            1     DIOXOLANE T/CN
E3            0 --> DIOXOLANE THYMINE/CN
E4            1     DIOXOLANE-1,2,6-HEXANETRIOL FORMAL-TRIOXANE COPOLYMER/CN
E5            1     DIOXOLANE-1,3,5-TRIOXANE COPOLYMER/CN
E6            1     DIOXOLANE-2,2-BIS(4-GLYCIDYLOXYPHENYL)PROPANE-TRIOXANE COPOL
                    YMER/CN
E7            1     DIOXOLANE-3,4-EPOXY-6-METHYLCYCLOHEXYLMETHYL 3,4-EPOXY-6-MET
                    HYLCYCLOHEXANECARBOXYLATE-TRIOXANE COPOLYMER/CN
E8            1     DIOXOLANE-ETHYLENE OXIDE-TETRAHYDROFURAN-TRIOXANE POLYMER/CN
E9            1     DIOXOLANE-ETHYLENE OXIDE-TRIOXANE COPOLYMER/CN
E10           1     DIOXOLANE-FORMALDEHYDE COPOLYMER/CN
E11           1     DIOXOLANE-FORMALDEHYDE POLYMER/CN
E12           1     DIOXOLANE-FORMALDEHYDE-POLYCAPROAMIDE POLYMER/CN

=>
Uploading C:\Program Files\STNEXP\Queries\10530088dioxolane.str
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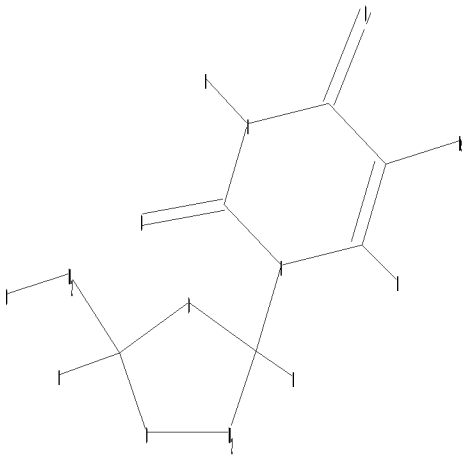
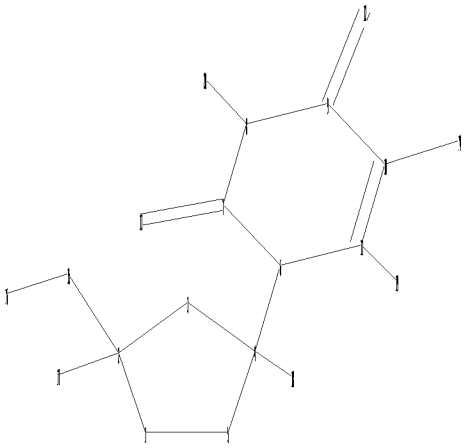




chain nodes :
12 13 14 15 16 17 18 19 20
ring nodes :
1 2 3 4 5 6 7 8 9 10 11
chain bonds :
2-15 2-17 4-6 4-18 7-13 8-20 9-12 10-14 11-19 15-16
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 6-7 6-11 7-8 7-13 8-9 9-10 9-12 10-11
exact bonds :
2-15 2-17 4-18 8-20 10-14 11-19 15-16

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 12:31:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 22 TO 418
PROJECTED ANSWERS: 8 TO 329

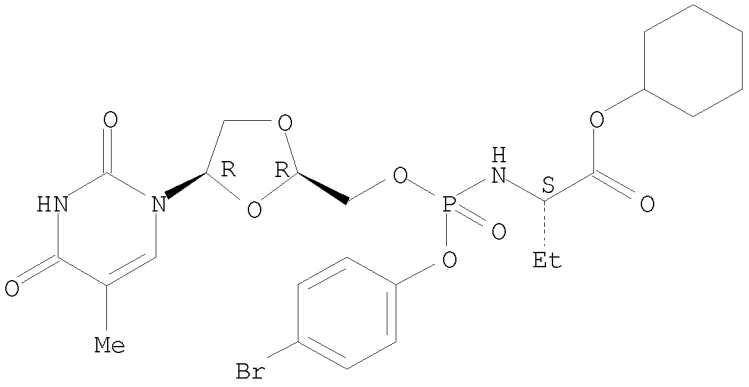
L2 8 SEA SSS SAM L1

=> d l2 scan

L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN Butanoic acid, 2-[[(4-bromophenoxy)[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-

dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]phosphinyl]amino]-,
cyclohexyl ester, (2S)-
MF C25 H33 Br N3 O9 P

Absolute stereochemistry.

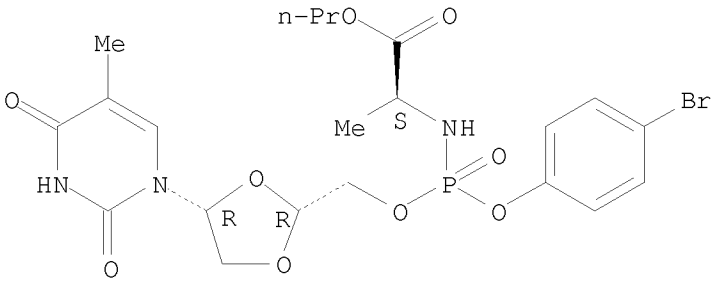


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN L-Alanine, N-[(4-bromophenoxy)[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-
1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]phosphinyl]-, propyl ester
MF C21 H27 Br N3 O9 P

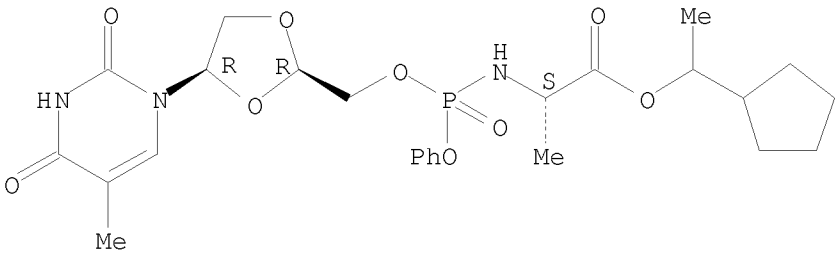
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN L-Alanine, N-[[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-
pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]phenoxyphosphinyl]-,
1-cyclopentylethyl ester
MF C25 H34 N3 O9 P

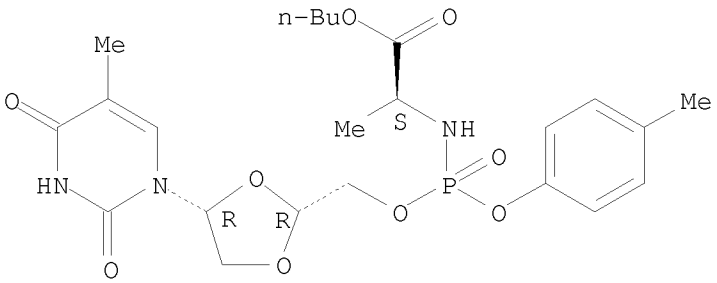
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN L-Alanine, N-[[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy](4-methylphenoxy)phosphinyl]-, butyl ester
MF C23 H32 N3 O9 P

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file stnguide

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.96	1.18

FILE 'STNGUIDE' ENTERED AT 12:31:38 ON 12 JUN 2009
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 5, 2009 (20090605/UP).

=>
Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.14	1.32

FILE 'REGISTRY' ENTERED AT 12:32:44 ON 12 JUN 2009

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUN 2009 HIGHEST RN 1155458-91-5
DICTIONARY FILE UPDATES: 10 JUN 2009 HIGHEST RN 1155458-91-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

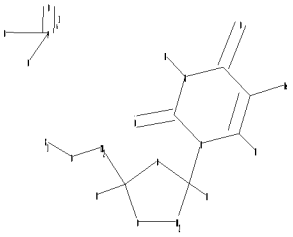
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

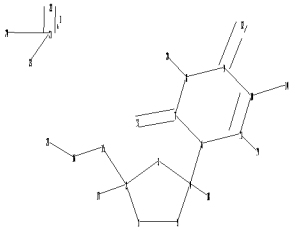
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\STNEXP\Queries\10530088dioxolane2.str





chain nodes :
12 13 14 15 16 17 18 19 20 21 22 23 24 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11
chain bonds :
2-15 2-17 4-6 4-18 7-13 8-20 9-12 10-14 11-19 15-16 16-27 21-22 21-23
21-24
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 6-7 6-11 7-8 7-13 8-9 9-10 9-12 10-11 16-27
21-22 21-23 21-24
exact bonds :
2-15 2-17 4-18 8-20 10-14 11-19 15-16

G1:C,H,[*1]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 27:CLASS

L3 STRUCTURE UPLOADED

```
=> s l3
SAMPLE SEARCH INITIATED 12:32:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       11 TO ITERATE

100.0% PROCESSED       11 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

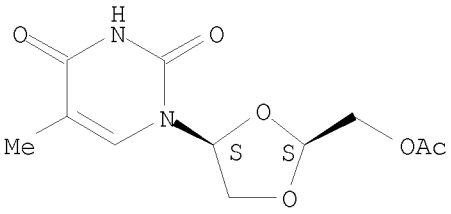
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           22 TO      418
PROJECTED ANSWERS:               1 TO       80

L4            1 SEA SSS SAM L3

=> d l4 scan

L4   1 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-[(acetyloxy)methyl]-1,3-dioxolan-
     4-yl]-5-methyl-, rel-
MF   C11 H14 N2 O6

Relative stereochemistry.
```




```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


ALL ANSWERS HAVE BEEN SCANNED


=> s l3 sss full
FULL SEARCH INITIATED 12:33:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      411 TO ITERATE

100.0% PROCESSED      411 ITERATIONS                                70 ANSWERS
SEARCH TIME: 00.00.01

L5           70 SEA SSS FUL L3

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   185.88     187.20

FILE 'HCAPLUS' ENTERED AT 12:33:09 ON 12 JUN 2009
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```

FILE COVERS 1907 - 12 Jun 2009 VOL 150 ISS 25
FILE LAST UPDATED: 11 Jun 2009 (20090611/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s l5/thu
            40 L5
       1134118 THU/RL
L6          16 L5/THU
                (L5 (L) THU/RL)

=> s HIV or (human immunodeficiency virus) or AIDS or K65R or M184V or T215Y
         85205 HIV
       2200854 HUMAN
         86717 IMMUNODEFICIENCY
        413899 VIRUS
         65720 HUMAN IMMUNODEFICIENCY VIRUS
                (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)
         79817 AIDS
           194 K65R
           407 M184V
           178 T215Y
L7      137840 HIV OR (HUMAN IMMUNODEFICIENCY VIRUS) OR AIDS OR K65R OR M184V
               OR T215Y

=> s l6 and l7
L8          14 L6 AND L7

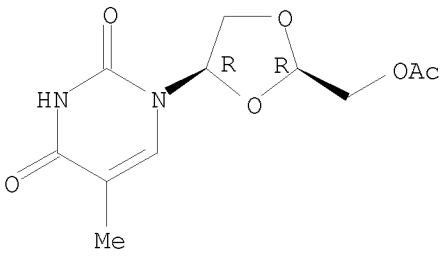
=> d l8 1-14 ti abs bib hitstr
```

L8 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI 5'-O-Aliphatic and amino acid ester prodrugs of
    (-)-β-D-(2R,4R)-dioxolane-thymine (DOT): Synthesis, anti- HIV
    activity, cytotoxicity and stability studies
AB A series of (-)-β-D-(2R,4R)-dioxolane-thymine-5'-O-aliphatic acid esters
    as well as amino acid esters were synthesized as prodrugs of
    (-)-β-D-(2R,4R)-dioxolane-thymine (DOT). The compds. were evaluated
    for anti-HIV activity against HIV-1LAI in human
    peripheral blood mononuclear (PBM) cells as well as for their cytotoxicity
    in PBM, CEM and Vero cells. Improved anti-HIV potency in vitro

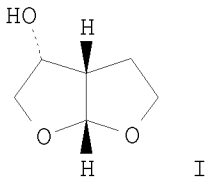
was observed for the compound 2-4 (5'-O-aliphatic acid esters) without increase in cytotoxicity in comparison to the parent drug. Chemical and enzymic hydrolysis of the prodrugs was also studied, in which the prodrugs exhibited good chemical stability with the half-lives from 3 h to 54 h at pH 2.0 and 7.4 phosphate buffer. However, the prodrugs were relatively labile to porcine esterase with the half-lives from 12.3 to 48.0 min.

AN 2009:137274 HCAPLUS <<LOGINID::20090612>>
DN 150:389124
TI 5'-O-Aliphatic and amino acid ester prodrugs of (-)-β-D-(2R,4R)-dioxolane-thymine (DOT): Synthesis, anti- HIV activity, cytotoxicity and stability studies
AU Liang, Yuzeng; Sharon, Ashoke; Grier, Jason P.; Rapp, Kimberly L.; Schinazi, Raymond F.; Chu, Chung K.
CS Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, The University of Georgia, Athens, GA, 30602, USA
SO Bioorganic & Medicinal Chemistry (2009), 17(3), 1404-1409
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier B.V.
DT Journal
LA English
IT 1138242-23-5P 1138242-24-6P 1138242-25-7P
1138242-26-8P 1138242-27-9P 1138242-28-0P
1138242-29-1P 1138242-30-4P 1138242-31-5P
1138242-32-6P 1138242-33-7P 1138242-34-8P
1138242-35-9P 1138242-36-0P 1138242-37-1P
1138242-38-2P 1138242-39-3P 1138242-40-6P
1138242-41-7P 1138242-42-8P 1138242-43-9P
1138242-44-0P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aliphatic and amino acid ester prodrugs of D-dioxolane-thymine: preparation, HIV antiviral, cytotoxicity and stability)
RN 1138242-23-5 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-[(acetyloxy)methyl]-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

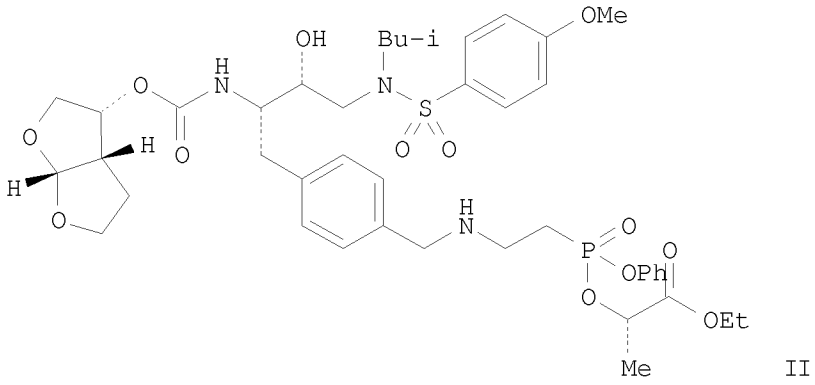
Absolute stereochemistry.



L8 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection
GI



I



II

AB A process for the synthesis of bisfuran intermediates, e.g., I useful for preparing antiviral HIV protease inhibitor compds. is hereby disclosed. Example compound II was prepared as adipic acid salt and succinic acid salts, using intermediate I as the key component in the preparation The invention compds. were evaluated for their HIV protease inhibitory activity (no data).

AN 2007:1275513 HCAPLUS <<LOGINID::20090612>>
DN 147:502340

TI Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection

IN Crawford, Kenneth R.; Dowdy, Eric D.; Gutierrez, Arnold; Polniaszek, Richard P.; Yu, Richard Hung Chiu
PA Gilead Sciences, Inc., USA

SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007126812	A2	20071108	WO 2007-US7564	20070329
	WO 2007126812	A3	20071221		
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	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
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	CA 2647316	A1	20071108	CA 2007-2647316	20070329
	US 20080004242	A1	20080103	US 2007-729522	20070329
	EP 1999133	A2	20081210	EP 2007-754134	20070329
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR				
	IN 2008DN07951	A	20081121	IN 2008-DN7951	20080922
	MX 2008012398	A	20081217	MX 2008-12398	20080926
	NO 2008004547	A	20081222	NO 2008-4547	20081028
	KR 2008108322	A	20081212	KR 2008-726569	20081029
	CN 101448838	A	20090603	CN 2007-80017888	20081117
PRAI	US 2006-787126P	P	20060329		
	WO 2007-US7564	W	20070329		

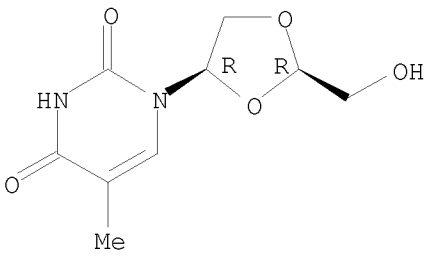
OS CASREACT 147:502340

IT 136982-89-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of carbamic acid bisfuranyl ester compds. as HIV protease inhibitors useful in treatment and prevention of retroviral infection)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Methods and kits for antiviral nucleoside combination dosing for treatment of viral infections

AB The invention is directed to methods and pharmaceutical kits for dosing a patient with antiviral nucleosides in an alternating manner.

AN 2007:966648 HCAPLUS <<LOGINID::20090612>>

DN 147:292175

TI Methods and kits for antiviral nucleoside combination dosing for treatment of viral infections

IN Erickson-Viitanen, Susan; Levy, Richard Steven

PA Pharmasset, Inc., USA

SO PCT Int. Appl., 98pp.
CODEN: PIXXD2

DT Patent

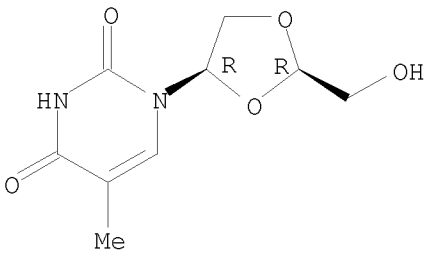
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007097991	A2	20070830	WO 2007-US4003	20070215
	WO 2007097991	A3	20080612		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,				

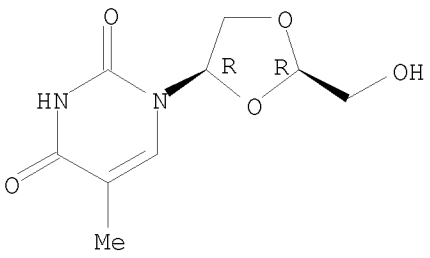
KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRAI US 2006-773997P P 20060216
OS MARPAT 147:292175
IT 136982-89-3 136982-89-3D, salts or prodrugs
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kits; methods and kits for antiviral nucleoside combination dosing for treatment of viral infections)
RN 136982-89-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 136982-89-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Methods for improving the pharmacokinetics of HIV integrase inhibitors by administering food and/or ritonavir
AB The invention provides methods for improving the pharmacokinetics of an HIV integrase inhibiting compound by administering food and/or ritonavir or a pharmaceutically acceptable salt thereof with the HIV integrase inhibitor. Agents and methods are provided that are useful for increasing the bioavailability or absorption of integrase

inhibitors, i.e., 4-oxoquinoline compds., such as 6-(3-chloro-2-fluorobenzyl)-1-((2S)-1-hydroxy-3-methylbutan-2-yl)-7-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (I) in order to increase their therapeutic effect in a patient. Thus, coadministration of I (100 mg twice daily) with ritonavir (100 mg twice daily) resulted in a net inhibition of I metabolism and significantly increased systemic exposures; thus, the data supported the use of low-dose ritonavir as a pharmacokinetic booster of I. Concurrent oral administration of I and ritonavir for up to 10 days was generally well-tolerated by patients, all adverse events were mild and transient.

AN 2007:760574 HCAPLUS <<LOGINID::20090612>>

DN 147:150815

TI Methods for improving the pharmacokinetics of HIV integrase inhibitors by administering food and/or ritonavir

IN Kearney, Brian P.; Kakee, Atsuyuki; Kawaguchi, Isao

PA Gilead Sciences, Inc., USA; Japan Tobacco, Inc.

SO PCT Int. Appl., 75pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007079260	A1	20070712	WO 2006-US49668	20061229
	WO 2007079260	A9	20070830		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	AU 2006332664	A1	20070712	AU 2006-332664	20061229
	CA 2635468	A1	20070712	CA 2006-2635468	20061229
	US 20070219243	A1	20070920	US 2006-647858	20061229
	EP 1976517	A1	20081008	EP 2006-848393	20061229
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
	IN 2008DN05576	A	20080926	IN 2008-DN5576	20080626
	MX 2008008494	A	20080715	MX 2008-8494	20080627
	KR 2008081358	A	20080909	KR 2008-718651	20080729
	NO 2008003333	A	20080929	NO 2008-3333	20080729
	CN 101336107	A	20081231	CN 2006-80052014	20080729
PRAI	US 2005-755039P	P	20051230		
	US 2006-756631P	P	20060106		
	US 2006-763901P	P	20060201		
	WO 2006-US49668	W	20061229		

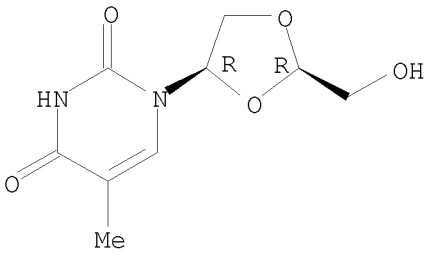
OS MARPAT 147:150815

IT 136982-89-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improving pharmacokinetics of HIV integrase inhibitors by administering food and/or ritonavir)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

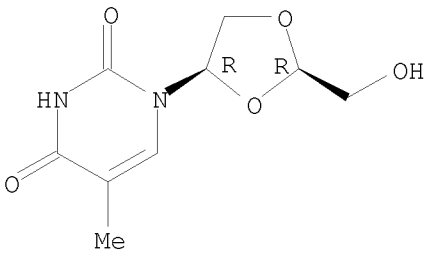


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Pharmacokinetics of the anti-human immunodeficiency virus agent 1-(β-D-Dioxolane)thymine in rhesus monkeys
AB β-D-Dioxolane-thymine (D-DOT) has potent and selective in vitro activity against several clin. important resistant human immunodeficiency virus (HIV) mutants and is in advanced preclin. development. Therefore, the single-dose i.v. and oral pharmacokinetics of D-DOT were studied with three rhesus monkeys. The pharmacokinetic profiles of D-DOT in serum and urine were adequately described by a two-compartment open pharmacokinetic model. D-DOT was rapidly and almost completely absorbed (absorption rate constant = 2.7 h-1; fraction of oral dose absorbed = 0.82 to 1.06). The average serum beta half-life was 2.16 h. The average central and steady-state vols. of distributions were 0.52 and 1.02 L/kg of body weight, resp., and the average systemic and renal clearance values were 0.36 L/h/kg and 0.18 L/h/kg. Four or eight percent of administered D-DOT was eliminated in the urine as glucuronide within 8 h after i.v. or oral administration, resp. D-DOT reached levels in the cerebrospinal fluid in excess of 10 to 20 times the median effective concentration for wild-type HIV and resistant mutants. The potent antiretroviral activity of D-DOT against a lamivudine- and zidovudine-resistant HIV-1 mutant, together with an excellent pharmacokinetic profile for rhesus monkeys, suggest that further development is warranted.
AN 2007:741992 HCAPLUS <<LOGINID::20090612>>
DN 147:291288
TI Pharmacokinetics of the anti-human immunodeficiency virus agent 1-(β-D-Dioxolane)thymine in rhesus monkeys
AU Asif, Ghazia; Hurwitz, Selwyn J.; Obikhod, Aleksandr; Delinsky, David; Narayanasamy, Janarthanan; Chu, Chung K.; McClure, Harold M.; Schinazi, Raymond F.
CS Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA
SO Antimicrobial Agents and Chemotherapy (2007), 51(7), 2424-2429
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
IT 136982-89-3
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics of D-DOT in rhesus monkeys)
RN 136982-89-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-

yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 44   THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

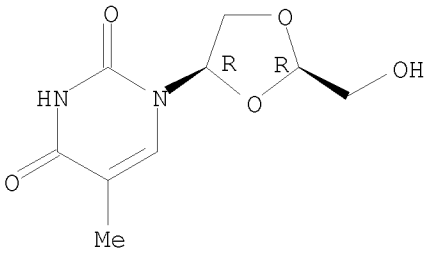
L8   ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI   Mechanism of action of (-)-(2R,4R)-1-(2-hydroxymethyl-1,3-dioxolan-4-yl)thymine as an anti-HIV agent
AB   (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine (DOT) is a thymidine analog that has potent in vitro activity against wild-type and nucleoside reverse transcriptase inhibitor (NRTI)-resistant HIV. For nucleoside analogs to inhibit viral replication, they must be metabolized to the active triphosphate, which inhibits the viral reverse transcriptase (RT). Using purified enzymes, the kinetics of DOT phosphorylation, inhibition of wild-type and drug-resistant HIV -1 reverse transcriptase activity, and excision of DOT-5'-monophosphate (DOT-MP) from a chain-terminated primer were examined DOT was phosphorylated by human thymidine kinase-1 (TK-1) but not by other pyrimidine nucleoside kinases, including the mitochondrial thymidine kinase (TK-2). Resistance to NRTIs involves decreased binding/incorporation and/or increased excision of the chain-terminating NRTI. RTs containing the D67N/K70R/T215Y/K219Q or T69S-SS/T215Y mutations show enhanced removal of DOT-MP from terminated primer as well as approx. four-fold decreased binding/incorporation. The Q151M and K65R mutations appear to cause decreased inhibition by DOT-TP. However, both the K65R and Q151M mutations show decreased excision, which would confer greater stability on the terminated primer. These opposing mechanisms could offset the overall resistance profile and susceptibility. Little or no resistance was observed with the enzymes harboring mutations resistant to lamivudine (M184V) and non-nucleoside RT inhibitors (K103N).
AN   2007:739016 HCAPLUS <<LOGINID::20090612>>
DN   147:268350
TI   Mechanism of action of (-)-(2R,4R)-1-(2-hydroxymethyl-1,3-dioxolan-4-yl)thymine as an anti-HIV agent
AU   Murakami, Eisuke; Bao, Haiying; Basavapathruni, Aravind; Bailey, Christopher M.; Du, Jinfa; Micolochick Steuer, Holly M.; Niu, Congrong; Whitaker, Tony; Anderson, Karen S.; Otto, Michael J.; Furman, Phillip A.
CS   Pharmasset Inc., Princeton, NJ, USA
SO   Antiviral Chemistry & Chemotherapy (2007), 18(2), 83-92
     CODEN: ACCHEH; ISSN: 0956-3202
PB   International Medical Press, Ltd.
DT   Journal
LA   English
IT   136982-89-3
     RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mechanism of action of (-)-(2R,4R)-1-(2-hydroxymethyl-1,3-dioxolan-4-yl)thymine as an anti-HIV agent)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)-β-D-(2R, 4R)-dioxolanethymine (DOT) and their anti- HIV activity

AB The synthesis, characterization, anti-HIV activity and cytotoxicity of dendrimers of (-)-β-D-(2R,4R)-dioxolane-thymine (DOT) and polyethylene glycol (PEG)-DOT conjugates are described. Dendrimers in this study were polyamidoamine (PAMAM) generation 2.0, 3.0, 5.0 and 6.0, along with 8.0-branched PEG with a mol. weight of 40 kDa. DOT was attached to PAMAM dendrimers or branched PEG via ester or phosphafte groups. Size exclusion chromatog. was used to purify the dendrimers and PEG conjugates, which were characterized by NMR and MALDI-TOF mass spectrometry. The synthesized PAMAM dendrimers and PEG conjugates were evaluated for anti-HIV activity against HIV-1LAI in primary human peripheral blood mononuclear cells (PBMCs) and cytotoxicity in PBMCs, CEM and Vero cells. PAMAM dendrimers of DOT with ester linkages and particularly phosphate linkers showed an increase in anti-HIV potency in comparison with DOT alone (140- and 56-fold, resp.). Unfortunately, the PAMAM dendrimers also exhibited increased cytotoxicity. Anti-HIV activity of PEG-DOT conjugates was found to be lower than that of DOT.

AN 2007:66477 HCAPLUS <<LOGINID::20090612>>

DN 146:350576

TI PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)-β-D-(2R, 4R)-dioxolanethymine (DOT) and their anti- HIV activity

AU Liang, Yuzeng; Narayanasamy, Janarthanan; Rapp, Kim L.; Schinazi, Raymond F.; Chu, Chung K.

CS The University of Georgia College of Pharmacy, Athens, GA, USA

SO Antiviral Chemistry & Chemotherapy (2006), 17(6), 321-329
CODEN: ACCHEH; ISSN: 0956-3202

PB International Medical Press, Ltd.

DT Journal

LA English

OS CASREACT 146:350576

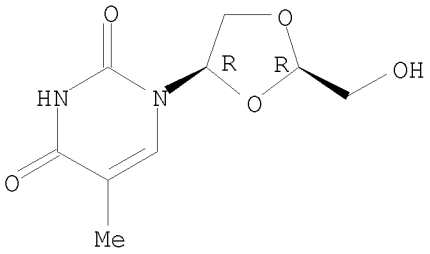
IT 136982-89-3DP, ethoxylated PAMAM conjugate derivs.
929705-97-5DP, ethoxylated PAMAM conjugate derivs.
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)-β-D-(2R, 4R)-dioxolanethymine (DOT) and their anti-HIV activity)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

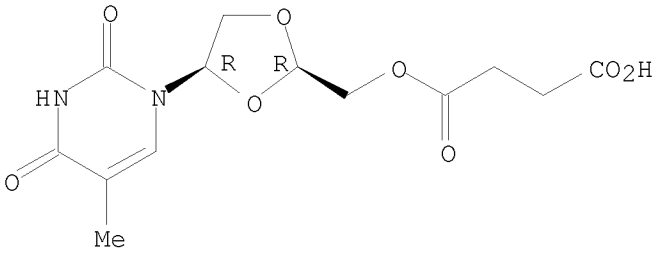
Absolute stereochemistry. Rotation (-).



RN 929705-97-5 HCAPLUS

CN Butanedioic acid, 1-[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] ester (CA INDEX NAME)

Absolute stereochemistry.

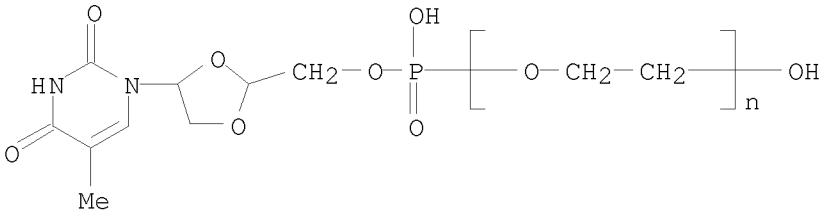


IT 929706-00-3P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)-β-D-(2R, 4R)-dioxolanethymine (DOT) and their anti-HIV activity)

RN 929706-00-3 HCAPLUS

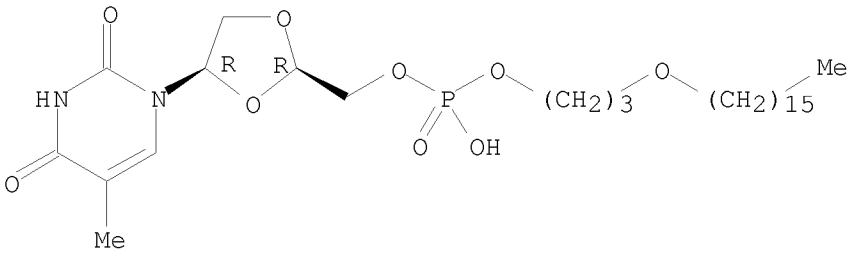
CN Poly(oxy-1,2-ethanediyl), α-[[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]hydroxyphosphinyl]-ω-hydroxy- (CA INDEX NAME)



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

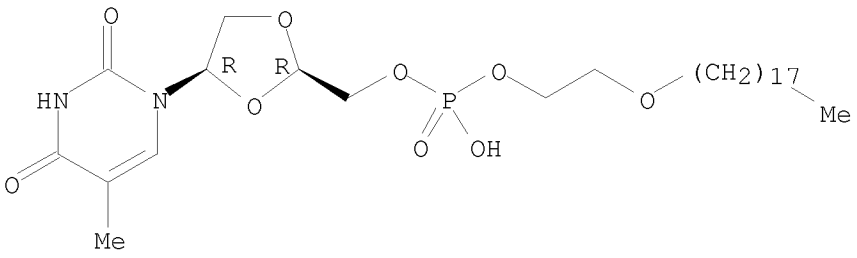
L8 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Phosphoramidate and phosphate prodrugs of (-)-β-D-(2R,4R)-dioxolane-thymine: Synthesis, anti- HIV activity and stability studies
AB A series of phosphoramidate and phosphate prodrugs of DOT were synthesized via dichlorophosphate or H-phosphonate chemical and evaluated for their anti-HIV activity against LAI M184V mutants in PBM cells as well as for their cytotoxicity. The antiviral and cytotoxic profiles of the prodrugs were compared with that of the parent compound (DOT), and it was found that four aryl phosphoramidates showed a significant enhancement (8- to 12-fold) in anti-HIV activity without cytotoxicity. Chemical stability of these prodrugs was evaluated in phosphate buffer at pH values of biol. relevance (i.e., pH 2.0 and 7.4). Enzymic hydrolysis was also studied in esterase or lipase in buffer solution Chemical stability studies indicate that the phosphoramidates have good chemical stability at pH 2.0 and at pH 7.4 phosphate buffer. Phosphoramidate prodrugs were hydrolyzed in vitro by esterase or lipase and found to be better substrates for lipases than for esterases. 1,3-Diol cyclic phosphates showed potent anti-HIV activity without increasing the cytotoxicity compared with that of DOT and have good chemical and enzymic stability. Long-chain lipid phosphates, although showed potent anti-HIV activity, exhibited increased cytotoxicity.
AN 2006:156931 HCAPLUS <<LOGINID::20090612>>
DN 144:403761
TI Phosphoramidate and phosphate prodrugs of (-)-β-D-(2R,4R)-dioxolane-thymine: Synthesis, anti- HIV activity and stability studies
AU Liang, Yuzeng; Narayanasamy, Janarthanan; Schinazi, Raymond F.; Chu, Chung K.
CS College of Pharmacy, The University of Georgia, Athens, GA, 30602, USA
SO Bioorganic & Medicinal Chemistry (2006), 14(7), 2178-2189
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:403761
IT 883989-33-1P 883989-34-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphoramidate and phosphate prodrugs of (-)-β-D-(2R,4R)-dioxolane-thymine and synthesis, anti- HIV activity and stability studies)
RN 883989-33-1 HCAPLUS
CN Phosphoric acid, mono[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] mono[3-(hexadecyloxy)propyl] ester (CA INDEX NAME)

Absolute stereochemistry.



RN 883989-34-2 HCAPLUS
CN Phosphoric acid, mono[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] mono[2-(octadecyloxy)ethyl] ester (CA INDEX NAME)

Absolute stereochemistry.

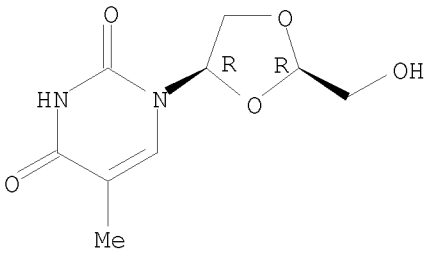


RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Anti-HIV Activity of (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine against Drug-Resistant HIV-1 Mutants and Studies of Its Molecular Mechanism
AB (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine (DOT) is the first thymidine kinase-activated nucleoside that is significantly active against all of the clin. significant NRTI-resistant HIV-1 mutants, including AZT (D67N/K70R/T215Y/K219Q), Tenofovir (K65R), and Lamivudine (M184V). To understand the mol. mechanism of drug resistance and the antiviral activity of DOT against drug-resistant RTs, mol. modeling studies of DOT-TP complexed with the wild-type (WT) and mutated RT were conducted. The key reason for this interesting antiviral activity profile is the presence of a dioxolane ring.
AN 2005:421890 HCAPLUS <<LOGINID::20090612>>
DN 143:90249
TI Anti-HIV Activity of (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine against Drug-Resistant HIV-1 Mutants and Studies of Its Molecular Mechanism
AU Chu, Chung K.; Yadav, Vikas; Chong, Youhoon H.; Schinazi, Raymond F.
CS College of Pharmacy, University of Georgia, Athens, GA, 30602, USA
SO Journal of Medicinal Chemistry (2005), 48(12), 3949-3952
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society

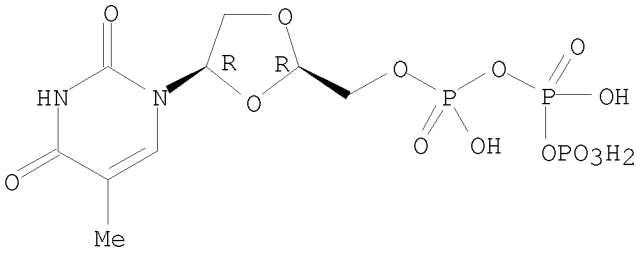
DT Journal
LA English
IT 136982-89-3 855138-64-6
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-HIV activity of (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine against drug-resistant HIV-1 mutants and studies of its mol. mechanism)
RN 136982-89-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



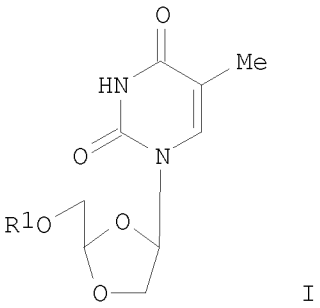
RN 855138-64-6 HCAPLUS
CN Triphosphoric acid, P-[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] ester (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Dioxolane thymine and combinations for use against 3TC/AZT resistant strains of HIV
GI



I

AB The present invention relates to the use of a dioxolane thymine compound according to the chemical structure of Formula (I): where R1 is H, an acyl group, a C1-C20 alkyl or ether group, a phosphate, diphosphate, triphosphate or phosphodiester group, for use in the treatment of HIV infections which exhibit resistance to 3TC and/or AZT. Preferably, compds. according to the present invention are combined with at least one anti-HIV agent which inhibits HIV by a mechanism other than through the inhibition of thymidine kinase (TK). These agents include those selected from among nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors, protease inhibitors, fusion inhibitors, among others. These agents are generally selected from the group consisting of 3TC (Lamivudine), AZT (Zidovudine), (-)-FTC, ddI (Didanosine), ddC (zalcitabine), abacavir (ABC), tenofovir (PMPA), D-D4FC (Reverset), D4T (Stavudine), Racivir, L-D4FC, NVP (Nevirapine), DLV (Delavirdine), EFV (Efavirenz), SQVM (Saquinavir mesylate), RTV (Ritonavir), IDV (Indinavir), SQV (Saquinavir), NFV (Nelfinavir), APV (Amprenavir), LPV (Lopinavir), fuseon and mixts. thereof. The TK dependent agents, such as AZT and D4T, may be used in combination with one of the dioloxane thymine compds. according to the present invention, but the use of such agents may be less preferred. In preferred compns. according to the present invention, R1 is preferably H or a C2-C18 acyl group or a monophosphate group. Pharmaceutical compns. and methods of reducing the likelihood that a patient at risk for contract an HIV infection will contract the infection are other aspects of the present invention.

AN 2004:513490 HCAPLUS <<LOGINID::20090612>>
DN 141:65057
TI Dioxolane thymine and combinations for use against 3TC/AZT resistant strains of HIV
IN Chu, Chung K.; Schinazi, Raymond F.
PA The University of Georgia Research Foundation, Inc., USA; Emory University
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004052296	A2	20040624	WO 2003-US39029	20031208
WO 2004052296	A3	20040923		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA	2502625	A1	20040624	CA 2003-2502625	20031208
AU	2003296360	A1	20040630	AU 2003-296360	20031208
EP	1569659	A2	20050907	EP 2003-812874	20031208

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR	2003017113	A	20051025	BR 2003-17113	20031208
CN	1723025	A	20060118	CN 2003-80105479	20031208
US	20050209196	A1	20050922	US 2005-530088	20050401
MX	2005003637	A	20050816	MX 2005-3637	20050405
IN	2005KN00698	A	20060224	IN 2005-KN698	20050421
PRAI US	2002-431812P	P	20021209		
	WO 2003-US39029	W	20031208		

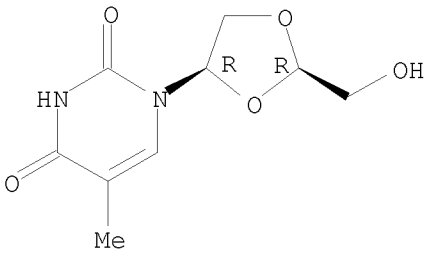
OS MARPAT 141:65057

IT 136982-89-3 136982-89-3D, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dioxolane thymine and combinations for use against 3TC/AZT resistant strains of HIV)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

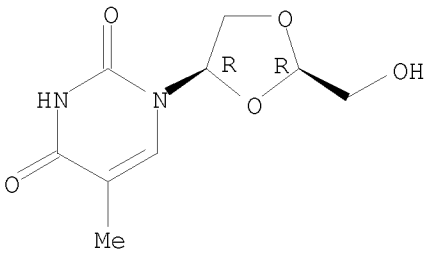
Absolute stereochemistry. Rotation (-).



RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Molecular mechanism of dioxolane nucleosides against 3TC resistant M184V mutant HIV

AB The mutation and resultant adaptability of HIV-1 reverse transcriptase (RT) present a major challenge to the design of the effective antiviral strategies because many initially potent drugs lose efficacy over time. Even though there is an urgent need for a comprehensive understanding of the mol. mechanism of anti-HIV drug resistance by mutant RTs, the unavailability of the structural information of the mutant RTs has prevented detailed investigations. In this study, the active site of the 3TC-resistant (M184V) RT is constructed by a computational method, which clearly shows that the side chain of Val184 occupies the binding site for the nucleoside triphosphates. Therefore, the distance between the side chain of Val184 and the sugar moiety of the nucleoside triphosphate must be closely related to the cross-resistance by M184V RT. The natural substrates, 2'-deoxyribo nucleoside triphosphates, escape from the steric stress from the bulky side chain of Val184 by virtue of the d-sugar conformation as well as the interaction of its 3'-OH group with Tyr115, which locates the nucleoside triphosphate out of the clashing distance from Val184. Similarly, the energy-minimized structures of various d-dioxolane nucleoside triphosphates (TP)/RT complexes indicate that the d-dioxolane sugar moiety acquires enough distance from Val184 due to the specific interaction of its 3'-oxygen atom with the nearby enzyme residues such as Tyr115 and Arg72.

AN 2004:489072 HCAPLUS <<LOGINID::20090612>>

DN 141:218359

TI Molecular mechanism of dioxolane nucleosides against 3TC resistant M184V mutant HIV

AU Chong, Youhoon; Chu, Chung K.

CS Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, The University of Georgia, Athens, GA, 30602, USA

SO Antiviral Research (2004), 63(1), 7-13
CODEN: ARSRDR; ISSN: 0166-3542

PB Elsevier Science B.V.

DT Journal

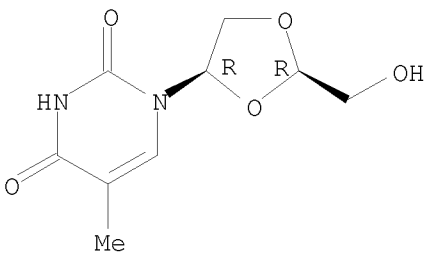
LA English

IT 136982-89-3
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. mechanism of dioxolane nucleosides against 3TC resistant M184V mutant HIV)

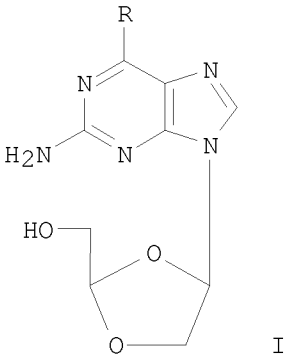
RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of enantiomerically pure β-D-dioxolane nucleosides as virucides
GI



I

AB A method and composition for the treatment of humans infected with HIV that includes the administration of an HIV treatment amount of an enantiomerically pure β-D-dioxolanyl purine nucleosides I wherein R is OH, Cl, NH2, or H, or a pharmaceutically acceptable salt or derivative of the compound, optionally in a pharmaceutically acceptable carrier or diluent. Thus, I (R = OH) was prepared and tested in human peripheral blood mononuclear cells for its antiviral activity (EC50 = 0.03μM). The toxicity of the compds. were evaluated in uninfected human PBM cells and showed no toxicity at a concentration of 100 μM.
AN 1999:450894 HCAPLUS <<LOGINID::20090612>>
DN 131:88137
TI Preparation of enantiomerically pure β-D-dioxolane nucleosides as virucides
IN Chu, Chung K.
PA Emory University, USA
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5925643	A	19990720	US 1992-935515	19920825
	US 5179104	A	19930112	US 1990-622762	19901205
	CA 2590125	A1	19920625	CA 1991-2590125	19911205
	EP 1164133	A2	20011219	EP 2001-203571	19911205
	EP 1164133	A3	20020102		
	EP 1164133	B1	20070801		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
	EP 1600448	A2	20051130	EP 2005-75365	19911205
	EP 1600448	A3	20060823		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
	EP 1693373	A1	20060823	EP 2005-77620	19911205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
	AT 368660	T	20070815	AT 2001-203571	19911205
	ES 2291268	T3	20080301	ES 2001-203571	19911205

	US 5444063	A	19950822	US 1992-967460	19921028
	WO 9404154	A1	19940303	WO 1993-US8044	19930825
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9350933	A	19940315	AU 1993-50933	19930825
	AU 670637	B2	19960725		
	EP 656778	A1	19950614	EP 1993-920366	19930825
	EP 656778	B1	20010530		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08501086	T	19960206	JP 1994-506616	19930825
	JP 3519736	B2	20040419		
	EP 1081148	A2	20010307	EP 2000-203932	19930825
	EP 1081148	A3	20030305		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, RO				
	ES 2157929	T3	20010901	ES 1993-920366	19930825
	JP 2002114787	A	20020416	JP 2001-251947	19930825
	CA 2143107	C	20041123	CA 1993-2143107	19930825
	US 5684010	A	19971104	US 1995-471533	19950606
	US 5767122	A	19980616	US 1995-469465	19950606
	AU 9716640	A	19970717	AU 1997-16640	19970327
	AU 714646	B2	20000106		
	US 5830898	A	19981103	US 1997-838072	19970415
	US 5834474	A	19981110	US 1997-839713	19970415
	JP 2001097973	A	20010410	JP 2000-246125	20000815
	JP 3881165	B2	20070214		
	GR 3036393	T3	20011130	GR 2001-401249	20010814
	AU 2003200421	A1	20030410	AU 2003-200421	20030207
	AU 2003200421	B2	20040408		
	JP 2004149543	A	20040527	JP 2003-414876	20031212
	JP 2007008959	A	20070118	JP 2006-263009	20060927
PRAI	US 1990-622762	A2	19901205		
	CA 1991-2099589	A3	19911205		
	EP 1992-902800	A3	19911205		
	EP 2001-203571	A3	19911205		
	JP 1992-502956	A3	19911205		
	US 1992-935515	A2	19920825		
	US 1992-967460	A3	19921028		
	AU 1993-50933	A3	19930825		
	EP 1993-920366	A3	19930825		
	JP 1994-506616	A3	19930825		
	WO 1993-US8044	W	19930825		
	US 1995-471533	A3	19950606		
	JP 2000-246125	A3	20000815		

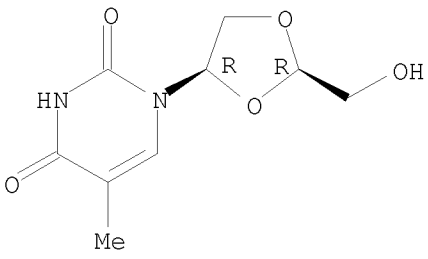
OS MARPAT 131:88137

IT 136982-89-3P 136982-90-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of enantiomerically pure dioxolane nucleosides as virucides)

RN 136982-89-3 HCAPLUS

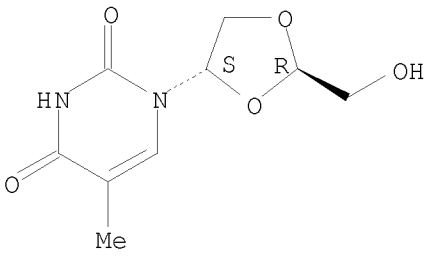
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 136982-90-6 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of antiviral 1,3-dioxolane nucleoside analogs
AB This invention includes the compds. 2'-deoxy-5-fluoro-3'-oxacytidines and pharmaceutically acceptable salts thereof for use in medical therapy, for example for the treatment or prophylaxis of an HIV infection (EC50 = 0.013-0.027 μM) with cytotoxicity of (IC50 < 1 μM).
AN 1999:17124 HCAPLUS <<LOGINID::20090612>>
DN 130:66736
TI Preparation of antiviral 1,3-dioxolane nucleoside analogs
IN Liotta, Dennis C.; Schinazi, Raymond F.; Choi, Woo-baeg
PA Emory University, USA
SO U.S., 16 pp., Cont.-in-part of U.S. 5,210,085.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5852027	A	19981222	US 1993-150012	19931109
	US 5210085	A	19930511	US 1991-659760	19910222
	US 5276151	A	19940104	US 1991-803028	19911206
	WO 9214729	A1	19920903	WO 1992-US1393	19920221
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 715577	B3	20000203	AU 1999-59571	19991119
	AU 2002300661	A1	20030220	AU 2002-300661	20020820
	AU 2002300661	B2	20060608		
PRAI	US 1991-659760	A2	19910222		

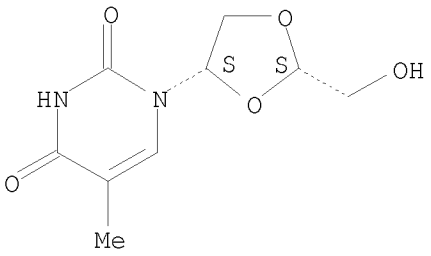
US 1991-736089 B2 19910726
US 1991-803028 A2 19911206
WO 1992-US1393 W 19920221
US 1990-473318 A2 19900201
US 1993-15992 A 19930210
AU 1999-44745 A3 19990826

IT 127658-07-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antiviral dioxolane nucleoside analogs)

RN 127658-07-5 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl-, rel- (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Synthesis and antiviral activity of 2'-deoxy-5-fluoro-3'-thiacytidine and nucleoside analogs

AB The present invention relates to a method of preparing the antiviral compds. 2'-deoxy-5-fluoro-3'-thiacytidine (FTC) and various prodrug analogs of FTC from inexpensive precursors with the option of introducing functionality as needed; methods of using these compds., particularly in the prevention and treatment of AIDS; and the compds. themselves. This synthetic route allows the stereoselective preparation of the biol. active isomer of these compds. and related compds. Thus, 2'-deoxy-5-fluoro-3'-thiacytidine was prepared and showed anti-HIV activity (EC50 = 0.011 μM) and cytotoxicity (IC50 > 100 μM) in human PBM cells.

AN 1998:15591 HCAPLUS <<LOGINID::20090612>>

DN 128:75640

OREF 128:14803a,14806a

TI Synthesis and antiviral activity of 2'-deoxy-5-fluoro-3'-thiacytidine and nucleoside analogs

IN Liotta, Dennis C.; Schinazi, Raymond F.; Choi, Woo-baeg

PA Emory University, USA

SO U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 402,730.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5700937	A	19971223	US 1995-481556	19950607
	US 5204466	A	19930420	US 1990-473318	19900201

	CA 2481078	A1	19910808	CA 1991-2481078	19910131
	EP 872237	A1	19981021	EP 1998-201737	19910131
	EP 872237	B1	20070117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 2001019690	A	20010123	JP 2000-160358	19910131
	JP 2002012591	A	20020115	JP 2001-151618	19910131
	JP 3530150	B2	20040524		
	EP 1772151	A2	20070411	EP 2006-77328	19910131
	EP 1772151	A3	20070613		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5210085	A	19930511	US 1991-659760	19910222
	US 6703396	B1	20040309	US 1995-402730	19950313
	US 5914400	A	19990622	US 1995-472345	19950607
	US 6153751	A	20001128	US 1999-337910	19990622
	AU 9944745	A	19991111	AU 1999-44745	19990826
	AU 715577	B3	20000203	AU 1999-59571	19991119
	JP 2001352997	A	20011225	JP 2001-151617	20010521
	JP 3844978	B2	20061115		
	AU 2002300661	A1	20030220	AU 2002-300661	20020820
	AU 2002300661	B2	20060608		
	JP 2005053893	A	20050303	JP 2004-146115	20040517
	JP 4108645	B2	20080625		
	JP 2006141408	A	20060608	JP 2006-33782	20060210
	AU 2006207874	A1	20060928	AU 2006-207874	20060907
PRAI	US 1990-473318	A2	19900201		
	US 1991-659760	A2	19910222		
	US 1991-736089	B1	19910726		
	US 1993-92248	B1	19930715		
	US 1995-402730	A2	19950313		
	AU 1991-73004	A3	19910131		
	CA 1991-2075189	A3	19910131		
	EP 1991-904454	A3	19910131		
	EP 1998-201737	A3	19910131		
	JP 1991-504897	A3	19910131		
	GB 1991-4741	A	19910306		
	GB 1991-9505	A	19910502		
	US 1993-15992	A1	19930210		
	US 1994-215498	B1	19940321		
	US 1995-472345	A1	19950607		
	AU 1999-44745	A3	19990826		
	JP 2001-151617	A3	20010521		
	AU 2002-300661	A3	20020820		

IT 127658-07-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and antiviral activity of 2'-deoxy-5-fluoro-3'-thiacytidine and nucleoside analogs)

RN 127658-07-5 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl-, rel- (CA INDEX NAME)

Relative stereochemistry.